EXHIBIT 7

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT RELATES TO:
Judkins v. Johnson & Johnson, et al.
3:19-cv-12430

MDL NO. 16-2738

RULE 26 EXPERT REPORT OF JUAN C. FELIX, MD

Date: 05/28/24

Juan C. Felix

Scope of Report

I was asked to review Ms. Anne Carter Judkins pathology and related records and provide my expert opinion on (1) diagnosis, (2) whether there is histologic evidence supporting internal exposure to talc-based body powder, and (3) the hypothesized link between the perineal use of talc and the development of ovarian cancer in general and, specifically, as it pertains to Ms. Judkins' ovarian cancer.

Background

I am a board-certified anatomic pathologist and cytopathologist with subspecialty expertise in gynecologic pathology. Since 2017, I have served as Chief of Anatomic Pathology, Professor and Vice Chair in the Department of Pathology of the Medical College of Wisconsin. Prior to moving to the Medical College of Wisconsin, I was Chief of Cytopathology at the Los Angeles County, University of Southern California Medical Center and Director of Gynecological Pathology at the Keck Medical Center of the University of Southern California. I received my Bachelors in Arts from Columbia College and my Medical Doctorate from Cornell University Medical College. I completed a residency in Anatomic Pathology and a Fellowship in Gynecological Pathology at the New York Hospital-Cornell Medical Center. I served two years as Assistant Professor at the New York Hospital-Cornell Medical Center and twenty-five years at the University of Southern California as Assistant, Associate and Full Professor. I directed one of the largest diagnostic centers in gynecological pathology in the United States and designed and founded two anatomic pathology laboratories, PathNet Esoteric Laboratory and the USC Outreach Lab. I am an internationally recognized expert in the field of diagnostic gynecologic pathology and am frequently consulted on challenging diagnostic cases by pathologists throughout the United States and internationally. Clinically, I continue to make diagnoses of gynecologic malignancies, including ovarian, uterine and cervical cancers, on a daily basis and discuss my findings with clinicians individually and as part of Tumor Boards. In this role, I participate in scholarly discussions regarding the etiology of gynecologic malignancies with subspecialists in the field. My research laboratory has collaborated in numerous projects pertaining to gynecological malignancies, including projects in the pathobiology of ovarian and uterine cancers. Further details of my professional career can be ascertained from my Curriculum Vitae, which is attached to this report (Exhibit A).

OVARIAN CANCER

Ovarian cancer is not a single disease, but includes numerous malignancies of varied origins, appearances, and behaviors. Ovarian cancer can be broadly classified into epithelial and non-epithelial ovarian cancer, based on the type of cells from which the tumors originate. Epithelial ovarian cancer is the most common type of ovarian cancer and encompasses many distinct tumor types, including serous (high-grade and low-grade), endometrioid, mucinous, clear cell, seromucinous, Brenner and mixed tumors. [WHO 2020]. For some of these tumors, there is a well-characterized precursor lesion, as is the case for endometrioid and clear cell carcinoma that arise from ectopic endometrial tissue (endometriosis and/or endometriomas) and serous carcinomas that arise from serous tubal intraepithelial carcinoma (STIC). [WHO 2020; Duska 2017]. Non-epithelial ovarian cancers include germ cell tumors and sex cord-stromal tumors and will not be discussed further in this report. [WHO 2020; Duska 2017]. Currently, the World Health Organization also recognizes a distinction between Borderline Ovarian Tumors and ovarian carcinomas and between Low-Grade Serous Carcinoma and High-Grade Serous Carcinomas. [WHO 2020]. This latter recognition is based on the different biological behavior between these groups as well as the clear difference in the types of genetic mutations characteristic of each. Additional information on the tumors discussed in this section can be found in the current WHO Classification of Female Genital Tumours (5th edition), Blaustein's Pathology of the Female Genital Tract (7th edition), and other related sources.

High-grade serous carcinoma is the most common form of ovarian cancer, representing about 70% of all ovarian malignancies. It is also the most deadly. About 80% of patients with high-grade serous carcinoma present with advanced disease (FIGO Stage III or IV) at a mean age of 65 years. These tumors arise from tubal-type epithelium, either in the ovary itself or in the fimbria (distal portion) of the fallopian tube. When discovered, the tumors generally have a solid and cystic appearance grossly and will usually have disseminated to the surface of other pelvic and abdominal organs. High-grade serous carcinomas have a

heterogeneous microscopic architecture with papillary, solid, and glandular growth patterns. Cytologically, the cells vary greatly in size, with markedly atypical and frequently bizarre nuclei usually with prominent macronucleoli. The immunohistochemical hallmark of high-grade serous carcinomas is the over-expression or complete lack of expression of p53 protein, indicating a mutation in the *TP53* gene.

Low-grade serous carcinomas are uncommon malignancies representing fewer than 5% of all ovarian cancer. The mean age at presentation is 43 years, more than a decade earlier than high-grade serous carcinomas. Low-grade serous carcinomas have been known to arise in women with prior serous borderline tumors and may represent a progression of a subset of these tumors. Whereas high-grade serous carcinomas are almost universally associated with *TP53* (p53) mutations, low-grade serous carcinomas lack the *TP53* mutation but frequently contain *BRAF* and *KRAS* mutations. [WHO 2020; Kurman 2013]. The tumors are frequently bilateral. Grossly, they are generally cystic with internal papillary projections. Some low-grade serous carcinomas have extremely numerous psammoma bodies, giving them a grossly gritty texture when incising them. Microscopically, the tumors exhibit a papillary architecture with frequent micropapillae and papillary budding. The tumor can cause desmoplasia of the surrounding stroma, although frequently little to no stromal reaction can be appreciated. Growth of micropapillae within unlined spaces is a characteristic, if not pathognomonic, feature. Cytologically, the nuclei are atypical to a degree similar to that of serous borderline tumors and to a much lesser degree than high-grade serous carcinomas. Lesser variation in size between nuclei, the absence of macronucleoli, and the lower mitotic rate all readily differentiate low- from high-grade serous carcinomas.

Endometrioid adenocarcinomas are the second-most-common carcinoma of the ovary, accounting for 15% of tumors, and occur at a mean age of 55 years. They can arise in younger patients, generally associated with Lynch syndrome and other mismatch repair gene mutations. Most tumors are thought to arise from endometriosis or in endometriomas, which have been shown to share common deleterious mutations with endometrioid adenocarcinomas in genes such as *ARID1A*, *PIK3CA*, *PTEN*, and *KRAS*. [WHO 2020; Bulun 2019]. The endometriotic cells appear to give rise to both endometrioid and clear cell carcinomas with endometrioid carcinomas sharing gene profiles with proloiferative endometrium such as low methylation of ESR1. [Beddows 2024]. As many as a quarter of endometrioid adenocarcinomas of the ovary will have a synchronous or metachronous endometrial adenocarcinoma. Endometrioid adenocarcinomas present as large unilateral tumors with a smooth external surface. On cut section, they are solid and cystic in appearance. Microscopically, endometrioid adenocarcinomas have a large variation in growth patterns. Although most will have the classic endometrioid glandular appearance resembling endometrial glands with cellular stratification and smooth luminal borders, they can be papillary or solid or mimic sex cord-stromal tumors. Cytologically, most endometrioid adenocarcinomas will exhibit moderate nuclear atypia with rounded, often vesicular nuclei. Marked atypia can be seen in higher-grade endometrioid adenocarcinomas but extreme atypia should trigger suspicion that the tumor may be serous in nature. Many endometrioid adenocarcinomas will exhibit squamous differentiation in the form of squamous metaplasia or squamous morules. Similarly, many will develop mucinous differentiation and may resemble a mucinous carcinoma in areas. Associations with small cell neuroendocrine carcinomas and undifferentiated carcinomas have been seen.

Clear cell carcinoma accounts for up to 10% of ovarian carcinomas and is strongly associated with the presence of endometriosis, and in particular endometriomas, where they can be seen arising from benign and then atypical endometriotic epithelium. As is the case with endometrioid carcinoma, clear cell carcinomas have been shown to share common deleterious mutations with endometriosis. [Bulun 2019]. Mean age of occurrence is 56 years. As with endometrioid adenocarcinomas, Lynch syndrome and other mismatch repair gene mutations predisposes to clear cell carcinomas. Clear cell carcinomas have alterations in the *ARID1A*, *PIK3CA*, *HNF1β* genes in over 50% of cases, and have significant prognostic differences from high-grade serous cancers. [Iida 2021 (citing Friedlander, Int J Gynecol Cancer. 2016 May;26(4):648-54)]. The endometriotic cell in clear cell carcinomas share molecular profiles with secretory endometrium such as high expressions of HNFB2. [Beddows 2024]. The tumors present as large unilateral masses with a smooth external capsule. On cut section the most common appearance is of a smooth dome-like projection into the lumen of an endometriotic cyst, although more solid tumors can occur. Microscopically, the tumor is characterized by its optically clear cytoplasm. The nuclei are generally

uniformly large, round and contain prominent nucleoli. Hyaline globules are frequently seen insinuated between tumor cells. The architecture is varied with papillary, tubulocystic, and solid areas.

Mucinous carcinoma of the ovary is uncommon, representing fewer than 4% of all ovarian malignancies. Their mean age of presentation is 55 years. Mucinous carcinomas are thought to arise mostly in mucinous borderline tumors, although they have also been postulated to arise in Brenner tumors and in mature cystic teratomas. Many mucinous carcinomas have mutations in *KRAS* and copy number loss of *CDKN2A*. *TP53* mutations are also common, occurring in over 60% of cases. The tumors present as large unilateral masses with smooth external capsules. Internally, they are frequently multicystic with viscous mucinous contents and areas of solid growth. Histologically, the tumors are heterogeneous, frequently displaying areas with a benign or borderline appearance in addition to frankly malignant areas that have markedly enlarged nuclei exhibiting marked atypia. Architecturally, most mucinous carcinomas exhibit a confluent, expansile glandular pattern, although infiltrative and papillary/cribriform patterns can also be seen. Distinction from metastatic carcinomas from the lower gastrointestinal tract is important and usually ascertained by immunohistochemical expression of CK 7.

Other EOC. Epithelial malignancies of other cell types occur with rarity in the ovaries. These include malignant Brenner tumors, mesonephric adenocarcinomas, small cell neuroendocrine carcinomas, small cell carcinomas, hypercalcemic type, and undifferentiated carcinomas. The rarity of these tumors precludes adequate assessment of their epidemiology, etiology, and pathogenesis.

Like most cancers, ovarian cancers develop as a result of genetic mutations, whether inherited or acquired. To date, old age, family history of ovarian or breast cancer, and inherited mutations in known cancer susceptibility genes are the strongest risk factors associated with the development of ovarian cancer. Almost 25% of women diagnosed with ovarian cancer carry germline mutations in cancer susceptibility genes, including *BRCA1* and *BRCA2*. [Walsh 2011]. Germline mutations in *BRCA1 and BRCA2* account for approximately 15% of germline mutations in ovarian cancer, with other ovarian cancer-associated genes (including *MLH1, MSH2, MSH6, PMS2, EPCAM, TP53, STK11, PALB2, BRIP1, RAD51C*, and *RAD51D*) contributing a smaller percentage of germline risk. [Norquist 2016]. Women with germline mutations in *BRCA1* and *BRCA2* have been shown to carry a lifetime risk of developing ovarian cancer of approximately 50% and 20%, respectively. [Kuchenbaecker 2017; Norquist 2016].

The development of ovarian cancers in women without a genetic predisposition, the so-called sporadic ovarian cancers, are likely the result of non-lethal mutations acquired as a result of normal cell replication. [Tomasetti 2017].

BRIEF CLINICAL HISTORY:

Ms. Anne Carter Judkins (DOB 09/19/56) is a 67 year-old woman diagnosed at age 60 with Stage IIB high-grade serous carcinoma (HGSC) of her right ovary, following evaluation for possible cystocele and uterine prolapse. [JudkinsC-MHMR-00289-00290, 00294-00295; JUDKINSC_DHMC_C_MDR_00002-00013, 00060-00069; JudkinsC-DHMCPath-00003-00006]. On December 30, 2016, Ms. Judkins underwent a hysterectomy with bilateral salpingo-oophorectomy, pelvic peritoneal biopsies, pelvic and para-aortic lymphadenectomy, and omental biopsy. [JUDKINSC_DHMC_C_MDR_00060-00062]. Her family history is unremarkable except for a paternal great aunt with breast cancer and a maternal uncle with kidney/bladder cancer. [JUDKINSC_NCCC_C_MDR00178-00184; Plaintiff Profile Form]. Genetic testing did not identify known pathogenic germline mutations in *ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, DICER1, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PMS2, RAD50, RAD51C, RAD51D, SMARCA4, STK11*, or *TP53*. [JUDKINSC_REC00003-00009]. Ms.s Judkins was found to have a variant of uncertain significance (VUS) in the *PTEN* gene, and results of tumor testing confirmed homologous recombination deficiencies (HRD). [JudkinsC-AGMR-00006-00020; JudkinsC-MGMR-00003-4; JudkinsC-DHMCMR-00572-00574]. Based on records available to me through early 2024, it appears Ms. Judkins has been without evidence of disease since her initial diagnosis and treatment. [JudkinsC-DHMCMR-01036-01039; JudkinsC-WHPIMMR-00220-00222].

EXAMINATION OF THE PATHOLOGY SLIDES:

I have reviewed the pathology report and slides from Dartmouth-Hitchcock Medical Center, labeled SP16-53498, from Ms. Judkins' December 30, 2016 hysterectomy, bilateral salpingo-oophorectomy, pelvic peritoneal biopsies, pelvic and para-aortic lymphadenectomy, and omental biopsy. The slides revealed HGSC arising in the right ovary and involving the serosa of the fallopian tube. The tumor exhibits areas of necrosis and aggregates of foamy histiocytes. Such necrosis may occur spontaneously in what is postulated as the tumor outgrowing its blood supply or as a result of intermittent ovarian torsion. Tumor was present in sections of a pelvic sigmoid adhesion but not found in sections of right pelvic lymph nodes, left pelvic lymph nodes, right para aortic lymph nodes, infracolic omentum, uterus cervix, left tube or left ovary. Ms. Judkins' tumor was a HGSC of the usual type and was not associated with granulomatous inflammation or a foreign body reaction. Although birefringent particles can be observed in Ms. Judkins' histology slides under polarized light, these particles are not demonstrably within macrophages or associated with a foreign body reaction. In the absence of such pathologic findings, the presence of this material in the processed tissue specimens does not support biologic exposure, but rather particulate artifact introduced during the extensive processing of the tissue for histology review.

I understand that Ms. Judkins alleges her use of talc-based body powder caused her to develop ovarian cancer. You have asked me to review the pathology for histologic evidence of exposure to foreign material, including talcum powder. There is none. It is well known that talc, like virtually any foreign body, will cause a foreign body granulomatous reaction when introduced into vital (living) tissue. [E.g., Shah 2017; Irving 2015; Reichert 2012; Ellis 1994; Hamilton 1984].[1] This reaction is formed predominantly by macrophages, foreign body giant cells, and lymphocytes. [Shah 2017; Reichert 2012; de Brito 2017; Perou 1973]. Scrutiny of Ms. Judkins' pathology slides, including both tumor and non-tumorous tissue, using routine light and polarized light microscopy, reveals a complete absence of this characteristic histologic reaction to talc (or other foreign material). Similarly, careful histologic examination revealed no evidence of asbestos exposure (i.e., ferruginous bodies or foreign body fibers consistent with asbestos) in Ms. Judkins' tissues.[2] It is important to note that the vast majority of tissue slides will have microscopic particulate matter that is highlighted under polarized light. In the absence of an associated foreign body reaction, including the presence of foreign body giant cells and/or particle-laden macrophages, neither of which was observed in this case, these particles are widely agreed by pathologists to be simple particulate contaminants introduced to the tissue at the time of surgical removal and/or tissue processing for histologic examination. Neither the operating room nor the histology laboratory are particle-free environments, and it is virtually impossible to prevent ubiquitous microscopic particulates from coming into contact with the lab instruments, containers, surfaces, reagents, and paraffin involved in the processing of surgical tissue specimens into pathology blocks and slides. [E.g., McDonald 2019, Ultrastruct Pathol; Perou 1973]. As expected, such particles are rarely encountered in some of Ms. Judkins' histology slides, but these particles are not confirmed to be talc, are not demonstrably in the plane of or associated with tissue, and uniformly lack the expected tissue reaction that would corroborate a true foreign body exposure.

TALC AND OVARIAN CANCER

While some retrospective case-control studies have suggested a weak association between perineal talc exposure and ovarian cancer (e.g., Cramer 2016; Harlow 1992), others have not, and analyses of prospective studies in four different cohorts have also failed to support an association. [O'Brien 2020;

[1] This property of talc is why it has been used for decades to obliterate the pleural space in patients with recurrent pleural effusions. Pertinently, there is no increase in the incidence of malignancy in patients who have been treated with pleurodesis. [Hunt 2007; Weissberg 1993].

[2] To the extent the plaintiff's experts claim that Ms. Judkins was exposed to asbestos through the use of contaminated talc body powder, epidemiologic studies do not support a causal association between talc body powder and gynecologic cancers. [E.g., O'Brien 2020 (ovarian), O'Brien 2021 (uterine), O'Brien 2021 (cervical)]. Further, associations reported in some studies involving high-level, occupational and/or environmental asbestos exposure, which is not alleged in this case, are questionable for a number of reasons, including small case numbers, lack of pathology review and histologic subtype analysis, tumor misclassification, and failure to control for known risk factors. [Reid 2011, Slomovitz 2020].

Gonzalez 2016; Houghton 2014; Gates 2010; Gertig 2000]. To date, a pathobiological explanation as to how talc might cause ovarian cancer is lacking. Studies relied on to support talc's hypothetical ability to migrate into the reproductive tract following perineal or body application are artificial, report inconsistent results, and do not attempt to address migration from the external perineum, which is the exposure at issue in these cases. The available literature is mainly in experimental animals. Most of these studies fail to reveal migration of talc to the upper genital tract despite suspending the talc in physiologic solutions and placing talc on the vaginal fornix, cervix, and into the endometrium. [Wehner 1986; Wehner 1985; Phillips 1978]. Only when talc was suspended in an emulsifier and injected into the uterus was talc found in the ovary. [Henderson 1986]. In contrast to studies injecting or directly introducing talc into the reproductive tract, lifetime daily dusting of talc to the whole body of rats found no evidence of talc in the ovaries or bursa. [Boorman 1995]. The study investigators noted "[s]ince the animals were exposed for 6 hr per day with talc covering the fur and cage bars, there was ample opportunity for perineal as well as oral and respiratory exposure." [Boorman 1995]. Studies reporting talc particles in gynecologic tissue are also unconvincing, as they fail to corroborate their findings with the expected histological response to talc, which is necessary to rule out specimen contamination as a likely alternative explanation for their findings. [E.g., McDonald 2019, Ultrastruct Pathol; McDonald 2019, AJCP; Campion 2018; Henderson 1979; Heller 1996, Henderson 1971]. Even assuming the findings do not represent contamination, they do not support perineal exposure to talc as the source for the particles observed in the tissue specimen. [E.g., Heller 1996]. Without evidence of a biologic response capable of driving carcinogenesis, the mere presence of a foreign particle in tissue cannot support causation. From a mechanistic standpoint, proponents of the talc-ovarian cancer hypothesis argue that talc induces an inflammatory response in tissue and that this inflammation can cause ovarian cancer. Although the effects of inflammation have been linked to the development of certain cancers, such as the case of ulcerative colitis and the development of colon cancer and the case of chronic skin ulcers and the development of squamous carcinoma of the skin, there is no evidence that these particular types of chronic inflammatory conditions are present in cases of ovarian cancer, and to date there has been no credible data showing the presence of these types of inflammatory conditions in the ovaries of women with history of perineal talc exposure. Importantly, the inflammatory response to talc is different than those described above—it is one of a granulomatous and foreign body giant cell type, which is not associated with chronic tissue destruction or the development of cancer. [E.g., Shah 2017; Irving 2015; Reichert 2012; Hunt 2007; de Brito 1994; Hamilton 1984]. In my experience reviewing tens of thousands of ovaries throughout my career as a gynecologic pathologist, I have never seen a granulomatous or foreign body response in gynecologic specimens associated with polarizable particles that could be consistent with talc since surgeons stopped using talc to lubricate surgical gloves. [Reichert 2012; Perou 1973]. Furthermore, there is no medical literature associating such a foreign body response with the development of any gynecologic malignancy, including ovarian cancer, despite the fact that many women who have had their ovaries biopsied or removed are likely to have used perineal talc at some point in their lives. [E.g., Houghton 2014; Cramer 2016].

OBSERVATIONAL DATA

Observational epidemiological studies represent an important methodological tool that uncovers associations between disease and possible causal factors. The strength of this type of study is in broadly defining factors that are statistically related to the disease and may be involved in causing the disease. Even when associations appear to be strong and reproducible throughout the medical literature, history has shown that these results can mislead us as to the cause of disease. One such example is that of the etiology of cervical cancer. By the 1970s, numerous studies demonstrated a positive association between Herpes simplex type II virus and cervical cancer. Kessler summarized these in his landmark review. [Kessler II 1974]. Choi and coworkers showed an increased relative risk for cervical cancer of 2.33 in women with antibodies to Herpes simplex type II virus over women without. [Choi 1977]. As late as the year 2000, in a study that included the true cause of cervical cancer (Human Papillomavirus, HPV) Viikki and coworkers found a stronger association between Herpes simplex II virus and cervical cancer (RR 12, CI 2.4-34) than for HPV (RR 5.5, CI 4.2-7.2). [Viikki 2000]. Finally, several investigators tried linking Herpes simplex with putative causal mechanisms and discovered associations between Herpes and increased cancer associated proteins. Aurelian and coworkers demonstrated increased oncogenic proteins ICP 10/AG-4 associated with Herpes simplex type II infection in women with cervical cancer and its precursor lesions. [Aurelian 1981]. Today we know that all of these associations, as strong and reproducible as they

were found to be in the literature, were incorrect, as the sole cause of cervical cancer is infection by Human Papillomavirus. [Wright 2003; Bosch 2002]. The case of Herpes simplex and cervical cancer is not unique; many other associations between putative causal agents and cancer that were suggested by observational studies have been eventually disproved.

While interesting, the association between perineal talc use and ovarian cancer reported in some retrospective case-control studies could be entirely coincidental. There are numerous explanations for such a coincidental association. For example, if the precursor lesions of ovarian cancer caused perineal itching, women might use talc in an attempt to soothe their discomfort. A causal mechanism between talc and ovarian cancer has never been established. I agree with the conclusions of Goodman and others that the weak statistical associations observed in some of the epidemiological case-control studies do not support a causal association between talc and ovarian cancer. [E.g., Goodman 2020; NCI 2024].

RESPONSES TO PLAINTIFF EXPERTS

In her expert report, Dr. Judith Wolf bases much of the reliance for her opinions on retrospective case-control studies while seeming to dismiss prospective cohort studies. This is somewhat puzzling since the scientific community considers prospective cohort studies to bea higher degree of evidence and, therefore, more reliable than case-control studies. When evaluating prospective cohort studies there is no association between talc use and the development of ovarian cancer. [O'Brien 2020; Gonzalez 2016; Houghton 2014; Gates 2010; Gertig 2000]. Dr. Wolf also highlights the mechanisms by which particulate matter might travel from the vagina to the peritoneal surfaces. While an interesting hypothetical, there is no data demonstrating the migration of talc (or other particulates) from the perineum to the ovarian or peritoneal surfaces. As noted above, talc is known to generate a vigorous foreign body response in living tissue, including peritoneum and ovarian tissue, and this type of response is not associated with an increased risk of malignancy. [E.g., Shah 2017; Irving 2015; Reichert 2012; Hunt 2007; de Brito 1994; Hamilton 1984]. Over the last 35 years, I have examined over 200,000 gynecologic cases and tens of thousands of ovaries. Despite the common use of perineal talc, I have not encountered talc foreign body reactions since surgeons stopped using talc and other powders as lubricants for surgical gloves. My substantial experience and the general absence of talc foreign body reactions reported in the published gynecologic literature do not support Dr. Wolf's migration theories and are evidence that real-world talc use does not result in ovarian or peritoneal exposure. Dr. Wolf's statements regarding inflammation are similarly lacking in support. Cell culture studies of potential cancer-causing inflammatory mediators must be validated in animal models and humans before any causal assumptions can be made. This is because cells in culture cannot replicate the complexity of the human immune response, which involves many different cell types and factors acting together in concert; what is positive under artificial lab conditions may not be positive at the tissue or organism level and/or may not produce the predicted end result. Inflammation in ovaries is extremely rare and virtually always associated with an infection. Examination of neoplastic and non-neoplastic ovaries virtually never identifies the type of destructive inflammation associated with carcinogenic stimuli. Finally, in her Bradford Hill analysis on analogy, Dr. Wolf makes several incorrect statements. For example, Dr. Wolf states that human papillomavirus (HPV) causes cervical cancer as a result of an inflammatory process initiated by the foreign agent. This is incorrect. HPV initiates cervical carcinogenesis by expressing viral proteins (E6 and E7) that inhibit several key antioncogenic proteins (pRB, p53) in host cells by binding to them and initiating unregulated cellular replication. HPV E6/E7 proteins also activate TERT, an enzyme critical in telomere elongation that aids in immortalizing the infected cells. None of these initiating events is related to inflammation. [Gupta 2018; Yim 2005]. Similarly, Dr. Wolf also claims that inflammation is the mechanism by which sun exposure causes skin cancer. This is a misunderstanding and oversimplification of UV-induced carcinogenesis. Dr. Wolf fails to appreciate that UV radiation is a strong mutagen that can act directly on DNA to induce mutations that may lead to cancer.

Dr. John Godleski selected eight of Ms. Judkins' tissue blocks (labeled SP16-53498 A2, D6, D7, E1, E2, G2, G5, and G6)) for the presence of talc. In his report, Dr. Godleski states that he used SEM/EDS to analyze the composition of 932 particles, none of which exhibited the expected Mg/Si ratio consistent with talc and only 17 (1.8%) of which were within +/- 5% of the proper Mg/Si ratio. Figure 1 of Dr. Godleski's report purports to illustrate his "key microscopic findings" in the case and includes photographs of two unidentified birefringent particles in Ms. Judkins' pathology specimens - one in ovarian stromal tissue and

one in a pelvic lymph node. As an initial matter, Dr. Godleski did not subject the birefringent material photographed in Figure 1 to SEM/EDS analysis to determine if it is compositionally consistent with talc or if, more likely, it is consistent with the 915 non-talc particles he identified in Ms. Judkins' pathology specimens, which represents more than 98% of the total particles analyzed. Second, regardless of composition, none of this material is contained within macrophages or otherwise associated with a foreign body reaction. This is extremely problematic to Dr. Godleski's exposure opinions, as foreign material present in living stromal or lymph node tissue would necessarily elicit such reactions. The complete absence of these expected tissue reactions indicates that the particles photographed in Figure 1 of Dr. Godleski's report are simple post-surgical contaminant introduced into the specimens when the tissues were surgically removed from Ms. Judkins and then handled, grossed, and processed for histology review.

Additional photomicrographs taken by Dr. Godleski but not included in his expert report were provided to me for review. Like the exemplar particles in Figure 1 of his report, none of the birefingent particles Dr. Godleski photographed in Ms. Judkins' histology slides was determined to be talc by compositional analysis, and none was contained in macrophages and/or associated with a foreign body reaction to corroborate a true exposure. These photos were taken by Dr. Godleski to support his exposure opinions, but instead confirm that the nature of the birefringent material in Ms. Judkins' histology is merely artifactual (i.e., material introduced into the tissue specimens during the handling, grossing and processing of the tissue for histology slides). Neither the operating room, transporting containers, grossing table in the pathology lab, nor the tissue processors or reagents used in preparing histology blocks and slides are designed to prevent particles of the size present in Dr. Godleski's photographs from getting into the excised tissue. The reason labs are not designed to prevent introduction of these particles into surgical tissue specimens is that their presence does not interfere with the pathologist's examination and eventual diagnosis, and measures to prevent introduction of these sort of ubiquitous microscopic contaminants would be prohibitively expensive while altogether unnecessary. Dr. Godleski's failure to address the absence of foreign body reactions in Ms. Judkins' tissue and to consider the well-known potential for post-surgical tissue contamination and processing artifact as a valid, alternative explanation for his findings calls the validity of his opinions on biologic exposure into serious question.

Dr. Godleski's claim that he "removes" contaminants from the tissue blocks by removing 50 microns of the block surface before SEM analysis ignores the fact that tissue specimens processed for histology are exposed sequentially to a number of organic compounds that permeate the tissue at the cellular level. These agents fix, dehydrate, and clear the tissue for infiltration with molten paraffin wax. The resulting paraffin tissue blocks can be sliced into very thin sections for microscopic analysis. This entire process allows any accompanying particulate matter to penetrate through and around cell membranes and to become embedded throughout the tissue and not just on the surface of the block. In addition, unless Dr. Godleski's lab is completely particulate-free, which it is not, the ubiquitous nature of airborne particulate matter would inevitably result in particles settling onto the recently shaved block surface.

Dr. Godleski uses SEM/EDS to determine the relative chemical composition of particulate material on the surface of the processed tissue specimens. His SEM images do not provide enough detail to identify the nature of the cells present near the particulate material being analyzed or whether the material is intracellular or eliciting a foreign body reaction. Without evidence of such a reaction, which would necessarily exist if the particle was present in vital tissue, Dr. Godleski cannot conclude that the material in the processed specimens represents a true biologic exposure, as opposed to post-surgical contamination, much less form a valid causation opinion regarding the material and Ms. Judkins' cancer.

CONCLUSIONS

Review of the medical records and the surgical pathology in this case confirms that Ms. Judkins had a Stage IIB HGSC of her right ovary. There is no evidence of talc related foreign body reactions in any of the tissues reviewed, which included tissues from the right and left ovaries and fallopian tubes, uterus, cervix, omentum and pelvic and para-aortic lymph nodes. In the absence of the expected immunologic response to foreign material, the 17 particles identified as talc by Dr. Godleski and other birefringent material observed in some of the pathology slides is most consistent with irrelevant contaminant introduced during

the extensive processing of the tissue for histologic review. Ms. Judkins' talc use played no role in her development of ovarian cancer.

The opinions that I have expressed in this letter are true to a reasonable degree of medical certainty and are based on my review of the relevant medical records and pathology in this case, knowledge of the medical literature, as well as my education, training and experience as a physician specializing in gynecological pathology. I reserve the right to supplement or amend these opinions upon review of additional medical records, pathology or other pertinent information. I also reserve the right to respond to any opinions or testimony provided at deposition and trial by plaintiff's experts. The references cited in this report include many of the sources I analyzed in forming my opinions, and the attached materials list (Exhibit B) includes additional sources I have considered, though it is impossible to identify every relevant publication or text I have reviewed throughout my career as a gynecologic pathologist.

My professional fees for the activities in this matter are divided as follows: I charge $600.00 per hour for evaluation of medical records, $800.00 per hour for deposition testimony and $7,000.00 per day for trial testimony. Cases in which I have had deposition testimony and or trial/arbitration testimony in the last four years are attached in a separate document. (Exhibit C).